

Goitre and hypothyroidism in the newborn after cutaneous absorption of iodine

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SUMMARY Iodine goitre and hypothyroidism in 5 newborn infants in an intensive care unit were induced by cutaneous absorption of iodine, after numerous skin applications of iodine alcohol. The infant's skin permeability allows severe iodine overloading of the thyroid, resulting in goitre and hypothyroidism. Ioduria should always be sought in a newborn infant showing hypothyroidism. Iodine should not be used as a skin disinfectant in young infants.

Goitre in the newborn infant resulting from maternal ingestion of iodine-containing drugs is a well-known condition (Job *et al.*, 1974). Parenteral sources of iodine have also led to thyroid insufficiency both in the infant (Mornex *et al.*, 1970) and in the fetus (Denavit *et al.*, 1977). We now describe thyroid disorder in 5 newborn infants who had been treated in an intensive care unit where iodine solutions were freely applied to sterilise the skin.

Patients and methods

Treatment of respiratory distress of the newborn requires many procedures such as umbilical catheterisation, collection of capillary blood from the heel, venepunctures, scalp vein infusions, and blood cultures. The number of such procedures for an infant under treatment totalled as many as 20 to 40 daily. The mean duration of iodine applications was 4.8 days. The skin sterilising solution used was 1% iodine alcohol, which is carefully washed off with simple alcohol. The hands of nurses and physicians are also disinfected with 3.9% iodine polyvidone solution. Newborns less than one month of age were studied. Any baby having x-ray examination which involved an iodine preparation was excluded. All mothers were checked for having taken iodine-containing drugs during pregnancy.

The infants were studied in the first 4 weeks and later at intervals varying between 1, 2, 3, and 6 months. Blood analyses (first between 7th and 29th days) were performed for thyroid-stimulating hormone (TSH), thyroxine iodine (T4 I), free

thyroxine index (FTI), triiodothyronine (T3), total blood iodine (TBI), and urine analysis for 24 hour ioduria (UI). T3 and TBI could not always be measured, due to the amount of blood required. TSH was measured by radioimmunoassay (normal range ≤ 1 ng/ml), as were T4 I, T3, and T3 test (resin T3 uptake *in vitro*). TBI and UI were measured by Technicon Autoanalyser. FTI was calculated.

When there was a palpable goitre and evidence of a disordered thyroid function, ^{99m}Tc technetium scintigraphy was performed.

Results

Our study included 30 newborns admitted to the intensive care unit during the first days of life for a variety of causes, most commonly either respiratory distress requiring intubation and ventilatory assistance, severe infection, or congenital surgical malformations. Bone maturation was normal in all cases and none showed clinical evidence of hypothyroidism. All 30 infants received skin disinfection repeatedly as previously described. 5 showed evidence of a thyroid disorder, the remaining 25 had no such evidence.

Table 1 gives the clinical findings, and Table 2 the hormonal and biochemical findings of the 5 infants with thyroid disorder. 3 infants had a birthweight < 2850 g. Enlargement of the thyroid gland was rarely marked, but the gland was always visible and palpable on careful examination with the neck hyperextended. Scintigraphy confirmed enlargement of the gland. Only in one (Case 5) was there a family history of thyroid disorder (an aunt of the father); the mother of Case 5 also had a small goitre without

Table 1 Clinical findings in 5 newborn infants with signs of hypothyroidism

Case no.	Sex	Birthweight (g)	Onset of disease	Stay in intensive care unit (d)	Hypertrophy of thyroid gland	Other findings	Duration of treatment (d)	Current status (last check)
1	M	2490	Periods of apnoea, day 4	7	+	EEG: 'Ondine' syndrome; low blood Mg	3 m	Complete remission (3 m)
2	M	3350	Streptococcus, septicaemia, and meningitis, 3 w	29	+		16	Complete remission (7 m)
3	F	2850	Tracheomalacia, asphyxia, day 2	2	+		14	Complete remission (9 m)
4	M	2200	Diaphragmatic hernia operated on at 6 h	8	±		15	Complete remission (5 m)
5	M	3300	Acute respiratory distress, day 1	12	+		16	Complete remission (6 m)

Table 2 Hormonal and biochemical findings in 5 newborn infants with signs of thyroid disorder

Case no.	Age (d)	TSH (ng/ml)	T4 I (μ g/100 ml)	FTI	T3 (ng/ml)	TBI (μ g/100 ml)	UI (mg/24 h)	T3 test
1	19	44	1.07	0.85	2.95		4.8	0.79
	2 m		6.6	6.01			0.021	0.90
	3 m	0.35				14.4	0.005	
2	27	21.7	0.88	0.82		8.4	0.648	0.93
	50	0.5	7.56	7.03		9.4	0.042	0.93
	10	1.58	4.87	4.63		425	3.6	0.95
3	38	0.61	6.49	6.85			0.006	0.98
	12	10.1					2.94	
	22	18	0.33	0.24	2.48		0.171	0.72
4	37		7.15	6.72			0.055	0.94
	55	1.0	7.88					
5	65	0.96	11.57	9.72				0.84
	30	14.79	1.27	1	3.05	28.5	0.137	0.79
	6 m	0.25	6.82	6.07			0.039	0.89

Conversion: Traditional units to SI—T4 I: 1 μ g/100 ml \approx 12.87 nmol/l. T3: 1 ng/ml \approx 1.536 nmol/l. TBI 1 μ g/100 ml \approx 78.8 nmol/l.

other clinical abnormality, and received no treatment. In Case 1 there were repeated severe attacks of apnoea, with a polygraphic record characteristic of the 'Ondine' syndrome; these receded after thyroid treatment (Chabrolle *et al.*, 1978). Goitre was always absent on the first neonatal examination, emphasising that the goitre was acquired and not congenital, as also confirmed by its disappearance after a short course of treatment. This consisted of lyophilised thyroid extract, 0.10 g/m² (corresponding to thyroxine 1 mg/m²) (see Table 1).

Hormonal and chemical signs of hypothyroidism were clear-cut in all 5 cases. Raised values of TSH are well documented as being the most reliable test for this condition. In Case 3 the value was borderline but the other 4 infants had very high values. The physiological high level of TSH at birth falls after a few days, usually 48 hours, and never then reaches the values observed in our study. In all cases the values normalised after treatment. Correlating with the high TSH values, T4 iodine values were very low

(Case 3 apart) and they also later normalised. The course of FTI paralleled these findings. T3 (3 cases) and T3 test (all cases) were in the normal range, which is not surprising in a recent process where T3 synthesis continues while T4 is severely depressed. We emphasise the extreme overloading of the organism by iodine, as seen by the rates of total blood iodine (3 cases) together with, in all cases, a gross ioduria, up to 3 and 4 mg/24 h (normal 0.037 mg); the normal range being reached only after from 1 to 3–6 months (see Table 2).

Of the other 25 infants submitted to the same procedures in the unit, none had clinical symptoms or goitre. We excluded 5 small preterms, though their hormonal values were similar (TSH was as low, T3 and T4 were first a little lower but rose later to reach the values of the other 20). In these other 20 infants no abnormal hormonal or chemical findings were observed at any time (Table 3) using the normal values given by O'Halloran and Webster (1972), Abuid *et al.* (1974), and Corcoran *et al.* (1977).

Table 3 Hormonal and biochemical findings in 20 newborn infants exposed to iodine but without signs of thyroid disorder

	TSH (ng/ml)	T4 I (µg/100 ml)	FTI	UI (mg/24 h)	T3 test
n	19	20	20	18	20
Mean	1.03	7.92	7.43	0.037	0.92
SD	0.46	2.70	2.40	0.043	0.14
SEM	0.11	0.604	0.54	0.010	0.031
Range	0.60-2.18	3.7-13.65	3.30-13.51	0.0025-0.14	0.49-1.16

Note: Too few measurements of T3 and TBI were made to include here.

Discussion

Newborn's skin permeability. In the newborn the skin layer is very thin and its well-known permeability (Nachman and Esterly, 1971; Solomon and Esterly, 1973) has been successfully used in the past with mercury inunction, but recently has led to the tragedy of hexachlorophene encephalopathy (Lampert *et al.*, 1973). Iodine crosses the skin readily (Boe and Wereide, 1970; Solomon and Esterly, 1973), and more so with erythema from friction of the skin. In our 5 cases there was gross ioduria, reaching 1000 times the normal. The other 20 infants had a normal level of ioduria (except 2) and no thyroid disorder. Individual differences in skin permeability may explain these differences.

Iodine remains an excellent antiseptic agent, active against bacteria, viruses, and fungi, but even when used with due caution it may still cause trouble (Savoie and Leger, 1977). Because the clinical symptoms of thyroid disorders are slight and not readily recognised, they may be much more frequent than generally thought, and we consider that the newborn infant should not be endangered by exposure to iodine used topically.

Acquired neonatal iodine goitre and hypothyroidism. A defence mechanism against iodine overload exists through the Wolff-Chaikoff process (Wolff, 1969; Ingbars and Woeber, 1974; Mace, 1977). Normally, after a halogen overload, the transformation of iodide into organic iodine is inhibited, and this leads to suppression of thyroid hormonogenesis. After a few days, hormone synthesis is resumed but the amount of iodide entering the gland is controlled. Should this control be deficient, the thyroid gland becomes saturated and no active hormone is formed (Mornex *et al.*, 1970). Such deficient regulation is likely to occur especially in the neonatal period. Different newborns react differently to such chemical stress. The duration and degree of the iodine uptake play an important part, but as shown recently (Konishi *et al.*, 1976), a constitutional predisposition, related to the HLA histocompatibility system, may be involved.

Development of an iodine goitre is also favoured

at this age by the raised level of TSH stimulated by thyroid-releasing hormone after birth. Thus iodine, if given in the very first days of life, penetrates the thyroid gland more easily and may prolong this physiological phase. Experiments in rats (Croughs and Visser, 1965) have resulted in goitre by iodine-fortified diets after TSH treatment. Raising TSH levels has also been advocated in the respiratory distress syndrome of the preterm newborn (Mace, 1977) and this could contribute to iodine sensitivity of the thyroid.

In summary, a common and apparently harmless practice results in a profound hormonal disorder. Although this appears to be reversible, thyroid disorder induced in the first days or weeks of life is not necessarily without long-term effects.

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References

- Abuid, J., Klein, A. H., Foley, T. P., and Larsen, P. R. (1974). Total and free triiodothyronine and thyroxine in early infancy. *Journal of Clinical Endocrinology and Metabolism*, **39**, 263-268.
- Boe, E. and Wereide, K. (1970). Increased protein bound iodine in the serum from topical use of iodochloro-hydroxyquinoleine (vioform). *Acta Dermatovenereologica*, **50**, 397-400.
- Chabrolle, J. P., Monod, N., Plouin, P., Leloch, H., De Montis, G., and Rossier, A. (1978). Surcharge iodée postnatale avec hypothyroïdie et pauses respiratoires: danger de l'application cutanée de produits iodés. *Archives Françaises de Pédiatrie* (in press).
- Corcoran, J. M., Eastman, C. J., Carter, J. N., and Lazarus, L. (1977). Circulating thyroid hormone levels in children. *Archives of Disease in Childhood*, **52**, 716-720.
- Croughs, W., and Visser, H. K. M. (1965). Familial iodide induced goitre: evidence of an abnormality in the pituitary thyroid homeostatic control. *Journal of Pediatrics*, **67**, 353-362.
- Denavit, M. F., Lecointre, Cl., Mallet, E., De Ménibus, Cl., and Rossier, A. (1977). Un accident de l'amniofoetographie: l'hypothyroïdie. *Archives Françaises de Pédiatrie*, **34**, 543-551.
- Ingbars, H., and Woeber, K. A. (1974). The thyroid gland. *Textbook of Endocrinology*, pp. 95-232. Ed. by R. H. Williams. Saunders, Philadelphia, London, Toronto.

- Job, J. C., Bocquentin, F., and Canlorbe, P. (1974). Les goitres du nouveau-né. *Archives Françaises de Pédiatrie*, **31**, 127-136.
- Konishi, J., Grumet, F. C., Payne, R. O., Mori, T., and Kriss, J. P. (1976). HLA antigens in Japanese patients with Graves' disease and Hashimoto's disease. (Abst.) *Premier Symposium International HLA et Maladies*, Vol. 1., p. 336. INSERM, Paris.
- Lampert, P., O'Brien, J., and Garret, R. (1973). Hexachlorophene encephalopathy. *Acta Neuropathologica*, **23**, 326-333.
- Mace, J. (1977). On the diagnosis of hypothyroidism in the early neonatal period. *Journal of Pediatrics*, **91**, 347-348.
- Mornex, R., Berthezene, F., and Briere, J. (1970). Mécanismes des goitres à l'iode. *Journées Endocrinologiques de la Pitié*, p. 129. Ed. by J. Decourt and G. Dreyfus. Expansion Scientifique Française, Paris.
- Nachman, R. L., and Esterly, N. B. (1971). Increased skin permeability in preterm infants. *Journal of Pediatrics*, **79**, 628-632.
- O'Halloran, M. T., and Webster, H. L. (1972). Thyroid function assays in infants. *Journal of Pediatrics*, **81**, 916-919.
- Savoie, J. C., and Leger, A. F. (1977). La pathologie thyroïdienne iatrogène. *Semaine des Hôpitaux de Paris*, **53**, 1411-1415.
- Solomon, L. M., and Esterly, N. B. (1973). *Neonatal Dermatology*. Saunders, Philadelphia, London, Toronto.
- Wolff, J. (1969). Iodine goiter and the pharmacological effect of excess iodide. *American Journal of Medicine*, **47**, 101-124.

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Note added in proof: Since the preparation of this article, Pyati *et al.* (1977, *Journal of Pediatrics*, **91**, 825-828) observed absorption of iodine in the neonate after topical use of povidone iodine. No significant alteration in thyroid function was seen, but they recommended caution.